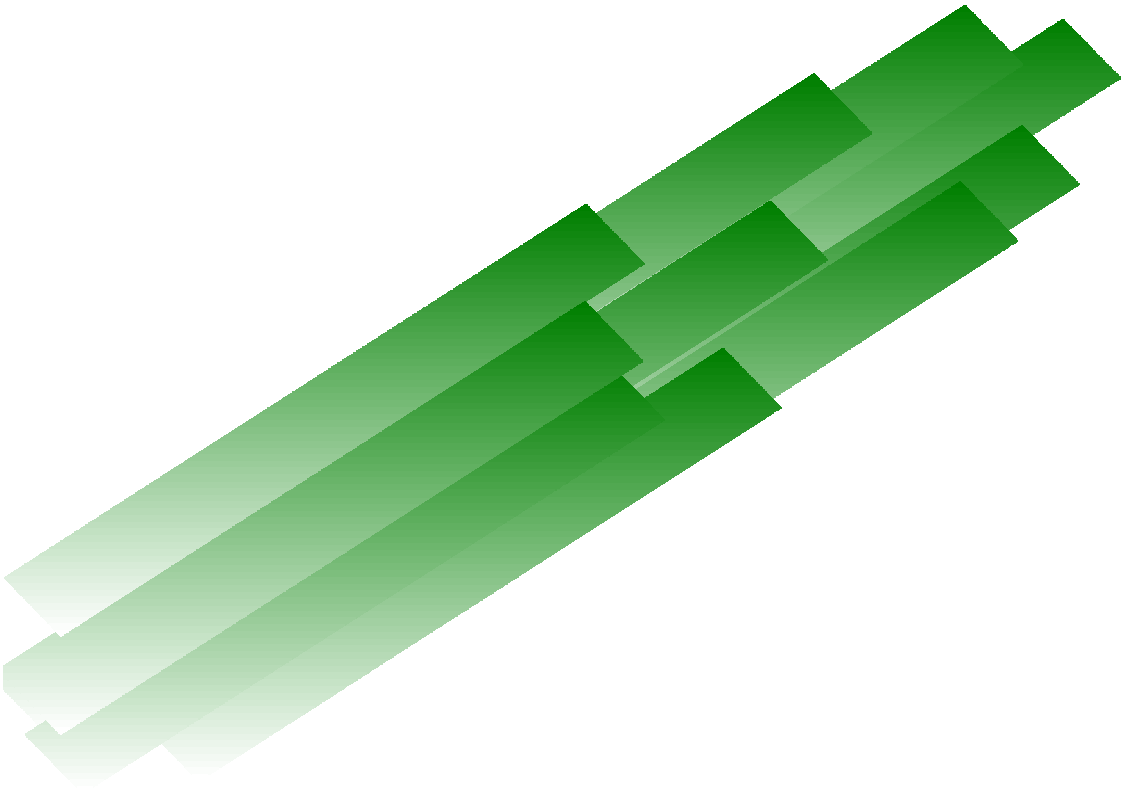
Guidance for Industry

Organization of an Abbreviated New Drug Application and an Abbreviated Antibiotic Application



U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
April 1997

OGD 1

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OGD 1

GUIDANCE FOR INDUSTRY[1]

ORGANIZATION OF AN ABBREVIATED NEW DRUG APPLICATION AND AN ABBREVIATED ANTIBIOTIC APPLICATION

I. INTRODUCTION

This guidance describes the recommended organization of abbreviated new drug applications (ANDAs) and abbreviated antibiotic applications (AADAs) and related submissions. Some ANDA and AADA submissions are difficult to review because they are complex, voluminous, or poorly organized. An application submitted with the proper jacket, organized with a clear table of contents and corresponding tabs, and with correct pagination makes the review process easier and more efficient. This guide summarizes one way an application can be organized that will be acceptable to the Food and Drug Administration (FDA). This guidance document replaces the Office of Generic Drugs Policy and Procedure Guide 30-91.

II. DEFINITIONS

A. Abbreviated Application

An application described under 21 CFR § 314.94, including all amendments and supplements to the application. The term applies to both abbreviated new drug applications and abbreviated antibiotic applications.

B. Archival Copy

A complete copy of the an abbreviated application intended to serve as the official reference source for the Agency.

C. Field Copy

A duplicate of the archival copy to be submitted to the applicant's home FDA District Office.

D. Review Copy

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[1]This guidance has been prepared by the Office of Generic Drugs in the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration. This guidance document represents the Agency's current thinking on the organization of an abbreviated application. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirement of the applicable statute, regulations, or both.

A duplicate of the archival copy for use by Agency reviewers.

III. POLICY

A. Archival, Review, and Field Copy

An ANDA and AADA applicant should submit archival, review, and field copies of the application in English.

The archival copy is a complete copy of an application and is intended to serve as the official reference source for the Agency. After an application is approved, the archival copy is retained by the Agency and serves as the sole file copy of the approved application. The review copy is destroyed. If there is a requirement for a bioequivalence study, then the review copy is divided into two parts containing the scientific information needed for FDA review of the application by different scientific reviewers. One part should contain information about chemistry, manufacturing and controls, and one part should contain information about bioavailability and bioequivalence.

Each part contains sections (e.g., "Labeling") that permit concurrent review of the application by various review disciplines. (See Review Copy--Additional Guidance for further explanation.)

An applicant may submit all or portions of the archival copy of the application in any form that the applicant and FDA agree is acceptable. Submission of electronic versions of the application are welcome, but should be discussed with the Office of Generic Drugs prior to actual submission.

Each application should be submitted in color-coded jackets. Information about the volume size and identification, the jacket specifications (including color coding), the size and quality of paper for text, and mailing instructions are shown in Attachment B.

B. Cover Letter

Each submission (whether original, amendment, supplement, or annual report) should include a dated cover letter with a clear, brief introductory statement. The cover letter should be on the letterhead of the applicant or the applicant's agent. If letterhead other than that of the applicant is used, an explanation of why the applicant's letterhead was not used should be included. The cover letter should assist the reviewer by including, at a minimum, the following:

1. Purpose of the submission;

2. Type of submission (ANDA, AADA, amendment, supplement, annual report, or resubmission as a result of prior withdrawal of an application);

3. Name, title, signature, and address of the applicant;

4. Proprietary name (if any) and established name of the drug product;

5. Number of volumes submitted.

For amendments, supplements, and annual reports, either the cover letter or the narrative for the section that was changed by the new submission should contain a description of the specific changes to previously submitted material. A comparison between the new information and the old information is preferred.

The cover letter should include a clear heading for special situations, such as: "Major" or "Minor" Amendment, or "Special Supplement--Changes Being Effected," or "Supplement--Expedited Review Requested."

C. Table of Contents

Each original application or other submission, as applicable, should include a table of contents. The purpose of the table of contents is to tell the reviewer where information can be found in the application. Attachment C provides a suggested table of contents for a typical ANDA. Attachment C is intended to complement the applicable regulations and can be used for general guidance in assembling the application, but should not be relied on solely for determining contents of the submission. Although not all sections apply to AADAs, this table of contents may be adjusted to accommodate the specific needs of the AADA.

If a section of the suggested table of contents is not used, insert a page behind the tab for that section (see below) and state "not applicable" in the table of contents and in the text. If a new subsection (line item within a section currently on the table of contents) is added to the table of contents, modify the application accordingly. Additional sections should be placed at the end of the table of contents and begin with number XXII (see suggested table of contents).

If the archival or review copy of the application requires more than one volume, the table of contents should be duplicated and placed in each volume. Thus, the same table of contents should be used in all jacketed volumes. (See Review Copy--Additional Guidance for further explanation regarding the separation of the review copy.)

D. Tabs

The contents of the submission should be organized by sections, and each section should be identified by a tab that corresponds to the section set forth in the table of contents. The tab shows the number and brief descriptive name of the section it identifies (e.g., Attachment C, "Section VI--Bioavailability/Bioequivalence"). Applicants may also use tabs for subsections within a section. In this event, use of a different color tab for subsections is useful. However, too many tabs may result in an unwieldy application.

E. Pagination

All pages of the archival copy of the application (except the tab pages) should be numbered in sequence. The sequence begins with page number one for the front side of the Application Form (Section I of Attachment C) and increases consecutively to the last page of the application. The sections and line items in the table of contents should accurately reflect the page numbers of the corresponding text.

The page number should be placed on the bottom center of each sheet of paper. Each submission after the original application (e.g., amendments or supplements) should also begin with page one and run consecutively to the end of that submission.

Correct pagination is essential to the reviewer in locating material in an application. Correct, consistent pagination between the text and the table of contents is especially important when an application consists of more than one volume.

F. Review Copy -- Additional Guidance

In addition to the archival copy, the applicant should submit a review copy. The review copy may contain two parts if bioavailability/ bioequivalence data is required, one part containing primarily chemistry, manufacturing, and controls data and the other part containing bioavailability/bioequivalence data. (Note that there will be gaps in the page numbering of the review copy if a bioavailability/bioequivalence part is required, since neither part contains all sections in the archival copy. See Attachment A.)

Each part may contain one or more volumes, depending on the size of the submission.

Each volume of the review copy should contain the complete table of contents, identical to that of the archival copy.

For identification purposes, the chemistry, manufacturing, and controls review part should be contained in a red jacket (or jackets), while the bioavailability/bioequivalence

review part should be contained in an orange jacket (or jackets).

Sections contained in the review copy should be identical to those of the archival copy, including use of the same page numbers.

For the typical ANDA (see Attachment C), both parts will contain Sections I through V, and VII. The chemistry, manufacturing, and controls part will also contain Sections VIII through XXI, and the bioavailability/bioequivalence part would contain Section VI (see Attachment A).

G. Field Copy--Additional Guidance

In addition to the archival copy, domestic applicants must submit a certification (21 CFR 314.94) that a "true" third/field copy of the technical sections (Chemistry, Manufacturing and Controls) of the application has been submitted to the appropriate FDA District Office.

Foreign applicants should submit the field copy to the Office of Generic Drugs. (See Attachment B for mailing address and specifications.)

ATTACHMENT A

COMPOSITION OF REVIEW COPIES

The following table illustrates the suggested separation of text for the "red" part of the review copy containing chemistry, and for the "orange" part of the review copy containing bioavailability/bioequivalence. The "sections" referred to are those shown on the suggested table of contents in Attachment C.

TABLE: COMPOSITION OF REVIEW COPIES CORRESPONDING TO SUGGESTED TABLE OF CONTENTS (ATTACHMENT C)

SECTION	RED COPY	ORANGE COPY
I	X	X
II	X	X
III	X	X
IV	X	X
V	X	X
VI (BIO)	-	X
VII	X	X
VIII - XXI	X	-

ATTACHMENT B

SUGGESTED SPECIFICATIONS

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1. VOLUME SIZE AND IDENTIFICATION

A. Each volume of an application should not be more than 3 inches thick.

B. The name and address of the applicant, the name of the drug, dosage form, and strength of the drug should be displayed on the front of the jacket of each volume.

C. Please do NOT number the volumes. The Agency will number the volumes.

D. All original abbreviated applications should be submitted in jackets. Small amendments or supplements not contained within jackets should be bound with fasteners (NO STAPLES) rather than by three-ring binders.

2. JACKET COLOR AND ORDERING

A. The volume jackets of the application should be color coded.

	Color	Form Number
Archival Copy	Blue	FDA 2626

Review Copy: (See Review Copy--Additional Guidance for further information.)

(l) Chemistry, Manufacturing and Controls (not containing Bio)

	Red	FDA 2626a

(2) Bioavailability/Bioequivalence

	Orange	FDA 2626c

Field Copy: (See Field Copy--Additional Guidance for further information.)

	Burgundy	FDA 2626h

B. A limited number of jackets may be obtained free of charge by sending a Special Order form (obtained from CFPDC--see below) that states the form number (as shown above), quantity, name, address and telephone number of requestor to:

Consolidated Forms and Publications Distribution Center
Washington Commerce Center
3222 Hubbard Road
Landover, Maryland 20785

Additional jackets, with the following specifications, may be purchased from a commercial source:

(l) Archival Copy

Polyvinyl type jacket .023 to .025 gauge
Front cover: 9" x ll-l/2"
Back cover: 9" x l2" with a full l/2" tab along the top edge.
Color: as stated above
Hidden reinforced l" hinges for front and back covers.
Rounded outside corners for front and back covers.

(2) Review Copy

Extra-heavy paper jacket
Front cover: 9" x ll-l/2"
Back cover: 9" x l2" with a full l/2" tab along the top edge.
Color: as stated above
Hidden reinforced l" hinges for front and back covers.
Rounded outside corners for front and back covers.

(3) Field Copy

Extra-heavy paper jacket
Front cover: 9" x ll-l/2"
Back cover: 9" x l2" with a full l/2" tab along the top edge.
Color: as stated above
Hidden reinforced l" hinges for front and back covers.
Rounded outside corners for front and back covers.

III. PAPER SIZE AND QUALITY

A. Good U. S. standard quality bond, 8-1/2" x ll", loose leaf paper.

B. Three-hole punched on left hand margin.

C. One-inch margins to accommodate readability after binding and photocopying.

D. Typing on both sides of paper is allowed if bleeding through the other side does not occur.

E. Paper should accommodate photocopying.

IV. MAILING

A. The packing carton should identify the contents by:

Drug name
Applicant's name
Applicant's address
"Archival Copy Enclosed" or "Review Copy Enclosed" (or both)

B. Mail abbreviated applications to:

Office of Generic Drugs
CDER, FDA
MPN II, HFD-600
7500 Standish Place
Rockville, MD 20855

C. Archival and review copies of abbreviated applications sent by overnight courier service or a parcel service should be sent to:

Office of Generic Drugs
CDER, FDA
Metro Park North II
7500 Standish Place, Room l50
Rockville, MD 20855

ATTACHMENT C

SUGGESTED TABLE OF CONTENTS

This suggested Table of Contents applies to an original abbreviated new drug application (ANDA). Although not all sections apply to an abbreviated antibiotic application (AADA), this table of contents may be adjusted to accommodate the specific needs of the AADA.

The page numbers shown, l-214, are for illustrative purposes, only.

Submitted [3l4.94(a)(11)]

3. Letters of Authorization (Two Copies) 214